REMARKS

With this amendment, Claims 44-47, 54-56, 60-65, 72-81, 88 – 92, 106-107, and new Claims 116-117 will be currently pending in the application. In this amendment, Claims 44, 63, and 79 are amended, Claims 108 through 115 have been withdrawn without prejudice, and new Claims 116 and 117 have been added to claim allowable subject matter. Support for the new claims is found throughout the specification. Favorable reconsideration is respectfully requested in light of the following Remarks.

Withdrawal of Claims 108-115

Applicant acknowledges the Examiner's comments with respect to the withdrawal of Claims 108-115 without prejudice to the later assertion of those claims.

Rejections of Claims 44-46, 54, 56, 60-65, 72-81, 88-92, 106 and 107 under Section 103(a)

The Office Action rejected Claims 44-46, 54, 56, 60-65, 72-81, 88-92, 106 and 107 under 35 U.S.C. Section 103(a) as being unpatentable over Oprandy et al., Journal of Clinical Microbiology, 1990 from Applicants' IDS ("Oprandy"), Huang et al., U.S. Patent no. 5,712,172 ("Huang"), Bulletin of World Health Organization, 1996, see IDS #5 ("WHO Bulletin"), Snowden et al., Journal of Immunological Methods, 1991, see IDS #5 ("Snowden"), Pawlak et al, U.S. Patent no. 5,770,460 ("Pawlak") and Hildreth et al., Journal of Clinical Microbiology, 1982 ("Hildreth"). Applicants traverse the rejection.

It is well known that "[t]o establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974)." M.P.E.P. § 2143.03. Accord. M.P.E.P. § 706.02(j). Moreover, the mere fact that references can be combined or modified does not render the resulting combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F2d 680, 16 U.S.P.Q 2d 1430 (Fed. Cir. 1990). To sustain an obviousness rejection, there must be a teaching or suggesting in the prior art to support the combination. It is appreciated that reasons or incentives must be provided in order to combine the cited references and it is impermissible to use the claimed invention as an instruction manual or "template" to piece together the teachings of the prior art so that the

claimed invention is rendered obvious. One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention. See *Ex parte Skinner*, 2 USPQ2d 1788 (B.P.A.I. 1986) and *In re Fritch*, 23 USPQ2d 1780 (Fed. Cir. 1992).

Applicants incorporate by reference and restate the text of their responses filed August 13, 2004, and June 10, 2005, as though fully set forth herein. Without prejudice, in this response, independent Claims 44, 63, and 79 have been amended, and new Claims 116-117 have been added. Applicants respectfully request reconsideration and allowance of the pending claims in light of the incorporated previous comments, the amendments set out herein, and the following comments.

At page 3, paragraph 3, of the Office Action, the Examiner states: "In this instant applicants are claiming a method of detecting an analyte." Applicants respectfully submit the Examiner's statement is an incomplete description of the invention as claimed. Instead, Applicants are claiming a method of analyzing an arthropod sample. As such, it encompasses more than the interaction between antibody and antigen, because first one or more epitopes on the target antigen must be exposed in a manner that does not adversely affect later antigen-antibody interactions within the single-step lateral flow format recited. The antigens of interest are contained initially within intact "blood-feeding" arthropods, such as mosquitoes or ticks. The challenge presented by and overcome by the present invention is to extract enough target antigen(s) from a rather "dirty" sample, representing a mixture of whole organisms (covered by exoskeleton) and human blood components, without significantly damaging the tertiary structure of the target antigen(s) so that the antibodies employed can function as intended. In the general description of the present invention found in the specification (at paragraph 0038 of the published application), Applicants teach the use of an "extraction solution or grinding solution" prior to testing; the extraction solution is described in detail in Example 3. Applicants further teach (at paragraph 69) the importance of compatibility of the extraction buffer with the other test reagents and materials that comprise the test. The extraction buffer must be capable of interrupting tissue and cellular structure to expose antigens contained within a sample comprising whole organisms, yet, the extraction buffer must not significantly interfere with the interaction between antigens and immobilized capture reagents and/or the integrity of immobilized capture reagents.

Neither Oprandy nor Hildreth teach such an extraction solution. Instead, Oprandy teaches only use of sodium dodecyl sulfate (SDS), an anionic detergent that is known to destroy the secondary and tertiary structure of proteins. SDS is not compatible with the lateral flow method claimed in the present application. Indeed, the references describing lateral flow devices cited by the Examiner do not suggest, teach or otherwise disclose the use of SDS in any of the reagents. Instead, a non-ionic detergent such as NP-40, Tween-20 or Triton X-100 is used in the present invention (see Example 3) during the grinding process. Non-ionic detergents are known to disrupt cell membranes and other cellular structures without denaturing protein structure.

Further, Hildreth does not teach the use of a non-ionic detergent during extraction or grinding. Specifically, at page 880, Hildreth states:

> "Pools were triturated with a mortar and pestle in 1.0 ml of PBS supplemented with 10% heat-inactivated fetal bovine serum, 500 U of penicillin, and 50 μg of streptomycin. Pools were centrifuged at 800 x g at 4°C for 20 min, and the supernatant fluid was collected and stored at –70°C."

Later, in describing EIA procedures, Hildreth teaches the use of a wash solution containing 0.05% Tween 20 and, also, the dilution of laboratory-raised mosquito pool samples with an incubation solution containing 0.1% Tween 20 (thus, resulting in a final concentration of less than 0.1% Tween 20), but the purpose of the non-ionic detergent as taught by Hildreth is to minimize non-specific binding of the antibody during EIA (see last sentence of the first paragraph of "Results" section). Such use of low-level non-ionic detergent was already known in the art for minimizing non-specific ("background") binding in immunoassays. Hildreth does not teach or otherwise disclose use of non-ionic detergents during the extraction process nor does Hildreth teach use of non-ionic detergents in immunoassays at a concentration of 0.1% or higher.

In contrast, the present application generally teaches the use of a non-ionic detergent in an extraction or grinding solution at a higher concentration than that taught by Hildreth, for example, at a concentration of about 0.5% as described in Example 3, and used during the extraction or grinding process, as shown in Figure 2.

The Examiner again asserts that it would have been obvious "to utilize the analyte detection reagents as taught by Oprandy et al. and/or Hildreth et al. and apply them to the

device taught by Huang et al., Pawlak et al., the WHO Bulletin and Snowden et al." However, not only do Oprandy and Hildreth fail to teach the use of an extraction or grinding buffer containing a non-ionic detergent at a concentration of at least 0.1%, neither demonstrates the adequacy of the disclosed reagents for testing field-collected, blood-engorged arthropods. In fact, Oprandy at page 1703 (first paragraph of Discussion) indicates the endogenous peroxidase activity of blood would interfere with the horseradish peroxidase reaction used for detection purposes. Hildreth teaches use of alkaline phosphatase with a chromogenic or fluorogenic substrate; it is not clear whether the system described by Hildreth is compatible for use with blood-engorged arthropods. Since the present invention is directed towards a simple method with commercial applications for field-testing blood-engorged arthropods, the deficiencies of Oprandy and Hildreth in this regard are significant. While Applicants admit there is prior art directed towards one-step immunoassay devices, no combination of the cited references teaches a method of obtaining an antigen-containing extract of field-collected, blood-engorged arthropods compatible for purposes of direct application to a one-step immunoassay device.

The citation to Pawlak does not cure the deficits in the other cited art, nor is there any motivation to combine it with any other reference. Pawlak not teach or disclose any relevant claim limitation, nor is there any teaching or disclosure, particularly of any enabling kind, of arthropod-based use. Instead, it appears that the language of the present claims has been used as a template to search the prior art and, applying this hindsight, argue that the claims are obvious, an approach that is not permissible.

For at least these reasons, Applicants respectfully request withdrawal of the rejection and allowance of Claims 44-46, 54, 56, 60-65, 72-81, 88-92, 106 and 107.

Rejections of Claims 44-47, 54, 56, 60-65, 72-81, 88-92, 106 and 107 under Section 103(a)

The Office Action also rejected Claims 44-47, 54, 56, 60-65, 72-81, 88-92, 106 and 107 under 35 U.S.C. Section 103(a) as being unpatentable over Oprandy, Huang, WHO Bulletin, Snowden, Pawlak, and Hildreth in view of Rattanarithikuln et al., American Journal of Tropical Medicine, 1996, from Applicants' IDS ("Rattanrithikuln") and Sithiprasasna et al., Annals of Tropical Medicine and Parasitology, from Applicants' IDS ("Sithiprasasna"). Applicants traverse the rejection.

The deficits of Oprandy, Huang, WHO Bulletin, Snowden, Pawlak, and Hildreth are discussed above, and the comments concerning same are incorporated herein. These deficits are not cured by combination with Rattanrithikuln nor Sithiprasasna. Because neither Rattanrithikuln nor Sithiprasasna discloses a method of analyzing an arthropod sample utilizing a grinding solution containing a non-ionic detergent at a concentration of at least 0.1%, the combination of references does not obviate the present invention for reasons discussed above. For at least these reasons, Applicants respectfully request that the rejection be withdrawn and that Claims 44-47, 54, 56, 60-65, 72-81, 88-92, 106 and 107 be allowed.

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PATENTS

CONCLUSION

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance. Favorable consideration and prompt allowance of the application is earnestly solicited.

Should Examiner Winkler believe anything further would be desirable in order to place the application in better condition for allowance, the Examiner is invited to contact the undersigned attorney at the telephone number listed below.

It is believed that any additional fees due with respect to this paper have already been identified. However, if any additional fees are required in connection with the filing of this paper, permission is given to charge account number 18-0013 under order no. 66011-0120, in the name of Rader, Fishman and Grauer PLLC.

Respectfully submitted,

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